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Pharmacokinetics and pharmacodynamics of two different landiolol formulations in a healthy Caucasian group.

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Abstract

BACKGROUND:

To date, no data have been reported on the pharmacokinetic and pharmacodynamic properties of landiolol, a fast-acting cardioselective β1-adrenergic antagonist, in non-Asian subjects. The aim of this study was to compare two landiolol formulations in healthy Caucasian subjects.

MATERIALS AND METHODS:

We conducted a single-center, prospective, double-blinded, randomized study in two cross-over periods with 12 healthy subjects (7 women and 5 men) each receiving three doses (0.1, 0.2, and 0.3mg/kg BW) of Onoact® 50 Lyophilized powder (50mg) or Rapibloc® concentrate IV (20mg/2mL) to evaluate the pharmacokinetics (PK), pharmacodynamics (PD), safety, and tolerability of the two landiolol formulations.

RESULTS:

For both formulations, maximum blood concentrations of landiolol were rapidly reached (median tmax 2.3±0.65 and 2.8±1.13min for the high dose of each formulation). The compounds had a short half-life (t1/2=3.2±1.2min and 3.0±1.1min for the low dose of the concentrate formulation and the lyophilized powder, respectively). The results showed no statistically significant differences between both formulations of landiolol for any PK parameters, at study doses. Both formulations dose-dependently and significantly decreased the heart rate values from 62.2bpm at baseline to minimum values of 55-56, 52-53, and 50-52bpm after 0.1, 0.2, and 0.3mg/kg respectively. This bradycardic effect was achieved within 1 to 3min. The decrease in systolic blood pressure (baseline: 107mmHg, minimum values were around 99mmHg) was significant but not dose dependent, and occurred within 3 to 12min. Seven mild to moderate AEs occurred after administration of the concentrate formulation. No SAEs were reported in this study.

CONCLUSION:

In Caucasians, both landiolol formulations showed similar pharmacokinetic behaviours, displaying very short half-lives (3.0 to 3.6min). In addition, after administration of both formulations, the landiolol-induced heart rate reduction showed fast onset and dose dependence, whilst the decrease of systolic blood pressure occurred more slowly, was less pronounced, and dose independent. In summary, both landiolol formulations delivered comparable plasma concentration profiles and showed good local tolerability. Overall, the pharmacokinetic and pharmacodynamic reactions observed in Caucasians were comparable to those described in Japanese subjects.

KEYWORDS:

Atrial fibrillation; Atrial flutter; Cardioselective β-blocker; Formulation; Heart rate; Landiolol; Sinus rhythm

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